8 March 2017
EMA/15862/2017
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant IgG degrading enzyme of *Streptococcus pyogenes* for the prevention of graft rejection following solid organ transplantation

On 12 January 2017, orphan designation (EU/3/16/1826) was granted by the European Commission to Hansa Medical AB, Sweden, for recombinant IgG degrading enzyme of *Streptococcus pyogenes* (also known as HMED-Ides) for the prevention of graft rejection following solid organ transplantation.

What is graft rejection following solid organ transplantation?

Graft rejection following solid organ transplantation is a problem that can occur when the recipient's body rejects the transplanted organ. Graft rejection is caused by the patient's immune system (the body's natural defences) recognising the transplanted graft as 'foreign' and attacking it. This results in inflammation and damage to the organs.

Graft rejection following solid organ transplantation is a life-threatening condition because the transplanted organ may fail and because medication is required to suppress the patient's immune system, which can result in infections and cancer.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients at risk of graft rejection following solid organ transplantation was estimated to be approximately 0.6 people in 10,000 in the European Union (EU). This was equivalent to a total of around 31,000 people[*], and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What methods of prevention are available?

At the time of designation, several medicines to suppress the immune system in order to prevent rejection after transplantation were authorised in the EU. These include the antibodies basiliximab and

[*]Disclaimer: For the purpose of the designation, the number of patients at risk of developing the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).

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antithymocyte immunoglobulin, calcineurin inhibitors such as ciclosporin or tacrolimus, azathioprine, mycophenolate mofetil and corticosteroids such as prednisolone or methylprednisolone.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients at risk of graft rejection following solid organ transplantation. Early studies showed that giving the medicine before kidney transplantation led to successful transplantation in patients with high levels of antibodies against the donor's organ. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

This medicine is made of an enzyme derived from the bacterium *Streptococcus pyogenes*, which breaks down antibodies called IgGs. IgGs are produced by the patient receiving the transplant against the transplanted organ. By breaking down IgGs, the medicine is expected to prevent the patient's immune system from attacking the transplanted organ, thereby reducing the risk that the organ will fail.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients at risk of graft rejection following solid organ transplantation were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for prevention of graft rejection following solid organ transplantation. Orphan designation of the medicine had been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 December 2016 recommending the granting of this designation.

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Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Recombinant IgG degrading enzyme of *Streptococcus pyogenes*	Prevention of graft rejection following solid organ transplantation
Bulgarian	Рекомбинантен ензим от *Streptococcus pyogenes*, разграждащ IgG	Предотвратяване на отхвърляне на присадката след трансплантация на солиден орган
Croatian	Rekombinantni enzim koji razgrađuje IgG-a potječe od *Streptococcus pyogenes*	Prevencija odbacivanja presatka nakon transplantacije solidnih organa
Czech	Rekombinantní IgG degradující enzym ze *Streptococcus pyogenes*	Prevence rejekce štěpu po transplantaci solidního orgánu
Danish	Rekombinant IgG-nedbrydende enzym i *Streptococcus pyogenes*	Forebyggelse af graftafstødning efter organtransplantation
Dutch	Recombinant IgG-afbrekend enzym van *Streptococcus pyogenes*	Preventie van transplantaatafstoting na soliede orgaantransplantatie
Estonian	Rekombinantne *Streptococcus pyogenes*'e IgG-degradeeriv ensüüm	Siirdorgani äratõukamise ennetamine pärast soliidorgani siirdamist
Finnish	Rekombinantti *Streptococcus pyogenes*-bakteerin IgG:tä hajottava entsyymi	Siirrännäisen hylkimisreaktion ehkäisy elinsiirron jälkeen
French	Enzyme recombinante de dégradation de IgG provenant de *Streptococcus* pyogènes	Prévention du rejet de greffe suite à la transplantation d'organes solides
German	Rekombinantes IgG-spaltendes Enzym von *Streptococcus pyogenes*	Prävention einer Abstoßungsreaktion nach Organtransplantation
Greek	Ανασυνδυασμένο ένζυμο αποικοδόμησης IgG του πυογόνου στρεπτόκοκκου	Πρόληψη της απόρριψης μοσχεύματος μετά την μεταμόσχευση στερεών οργάνων
Hungarian	*Streptococcus pyogenes* rekombináns IgG-t bontó enzimje	Szervtranszplantációt követő graft kilökődés megelőzése
Italian	Enzima ricombinante di streptococco piogene degradante le IgG	Prevenzione del rigetto di trapianto in seguito a trapianto di organi solidi
Latvian	Rekombinants IgG degradējošs *Streptococcus pyogenes* enzīms	Transplantāta atgrūšanas profilaksei pēc orgāna transplantācijas
Lithuanian	Rekombinantinis IgGskaidantis *Streptococcus pyogenes* fermentas	Transplantato atmetimo prevencija po parenchiminio organo transplantacijos
Maltese	Enzima ta' degradazzjoni tal-IgG rikombinanti ta' *Streptococcus pyogenes*	Prevenzjoni ta’ rifjut ta’ trapjant wara trapjant ta' organu solidu
Polish	Rekombinowany enzym degradujący IgG, pochodzący od *Streptococcus pyogenes*	Zapobieganie odrzuceniu przeszczepu po transplantacji narządów litych
Portuguese	Enzima recombinante do *Streptococcus pyogenes* que degrada a IgG	Prevenção da rejeição de enxertos após transplante de órgãos sólidos
Romanian	Enzimă recombinantă care degradează IgG provenită de la *Streptococcus pyogenes*	Prevenirea rejetului de grefăpost transplant de organe solide

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Rekombinantná IgG degradujúca enzým *Streptococcus pyogenes*	Prevencia odvrhnutia štepu po transplantácii solidného orgánu
Slovenian	Rekombinantni encim *Streptococcus pyogenes*, ki povzroča razpad IgG	Preprečevanje zavrnitve presadka po transplantaciji čvrstih organov
Spanish	Recombinante enzima de *Streptococcus pyogenes* que degrada la IgG	Prevención del rechazo de injerto después de trasplante de órgano sólido
Swedish	Rekombinant IgG-nedbrytande enzym från *Streptococcus pyogenes*	Förebyggande av transplantatrejektion efter solid organtransplantation
Norwegian	Rekombinant IgG-nedbrytende enzym fra *Streptococcus pyogenes*	Forebygging av transplantatavstøtning etter transplantasjon av solid organ
Icelandic	Raðbrigða ensím úr *Streptococcus pyogenes* sem brýtur niður IgG	Til að koma í veg fyrir höfnun eftir líffæraígræðslu